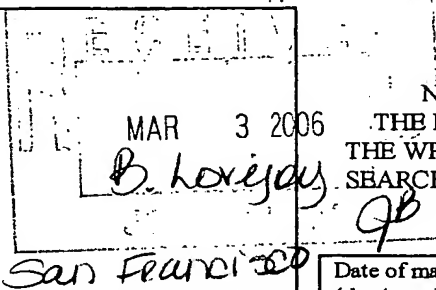


# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
BRETT A LOVEJOY  
JONES DAY  
222 EAST 41ST STREET  
NEW YORK, NY 10017-6702



## PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
(day/month/year) **24 FEB 2006**

Applicant's or agent's file reference  
11548-02-228 ✓

**FOR FURTHER ACTION** See paragraphs 1 and 4 below

International application No.  
PCT/US04/24752 ✓

International filing date  
(day/month/year) 30 July 2004 (30.07.2004)

Applicant  
DNA TWOPOINTTO INC.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70.

For more detailed instructions, see the notes on the accompanying sheet.

*Amend Prior to Pub 4-24-0  
Check U.S. IDS Refs 5-24-0  
Response to Written  
Opinion 5-24-06.*

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/ US  
Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (571) 273-3201

Authorized officer

Michael Borin

Telephone No. ((571) 272-054

Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|   |  |   |
|---|--|---|
| Applicant's or agent's file reference<br>11548-02-228 | <b>FOR FURTHER ACTION</b><br><small>see Form PCT/ISA/220<br/>as well as, where applicable, item 5 below.</small> |   |
| International application No.<br>PCT/US04/24752       | International filing date ( <i>day/month/year</i> )<br>30 July 2004 (30.07.2004)                                 | (Earliest) Priority Date ( <i>day/month/year</i> )<br>01 August 2003 (01.08.2003) |
| Applicant<br>DNA TWOPOINTTO INC.                      |  |   |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

a. With regard to the language, the international search was carried out on the basis of:



the international application in the language in which it was filed.



a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box No. II)

3. ☒ Unity of invention is lacking (See Box No. III)

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.



none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/24752

### Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-54

Remark on Protest

☐

The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐

The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☒

No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No. ....

PCT/US04/24752

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N33/00, 48

US CL : 702/19,27

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 702/19,27

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| X          | Schneider G. Peptide design by artificial neural networks and computer-based evolutionary search . Biochemistry, October 13, 1998, Vol. 95, Issue 21, 12179-12184 | 1-54                  |
| X          | US 2002/0177170 (LUO et al) 11/28/2002  | 1-54                  |
| X          | US 20020119492 A1 (CHIRINO et al), August 29, 2002  | 1-54                  |

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

|   |  |
|---|--|
| * Special categories of cited documents:  |  |
| "A" document defining the general state of the art which is not considered to be of particular relevance  | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "B" earlier application or patent published on or after the international filing date   | "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "O" document referring to an oral disclosure, use, exhibition or other means  | "&" document member of the same patent family  |
| "P" document published prior to the international filing date but later than the priority date claimed  |  |

Date of the actual completion of the international search

02 December 2005 (02.12.2005)

Date of mailing of the international search report

24 FEB 2006

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Authorized officer

Michael Borin

Telephone No. ((571) 272-054

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/24752

## BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group I, claims 1-54, drawn to method for constructing set of variants of biopolimer.

Group II, claims 59,65, drawn to variant set, or components thereof, obtained according to claim 1 or 6.

Group III, claims 58,64, drawn to nucleic acids encoding variants obtained according to claim 1 or 6.

Group IV, claims 66,67,72,73, drawn to cells containing variants obtained according to claim 1 or 6 or containing polynucleotides encoding therefor.

Group V, claims 55-57,61, drawn to variant set, or components thereof, obtained according to claim 2.

Group VI, claim 60, drawn to nucleic acids encoding variants obtained according to claim 2.

Group VII, claims 68,69, drawn to cells containing variants obtained according to claim 2 or containing polynucleotides encoding therefor.

Group VIII, claims 63, drawn to variant set, or components thereof, obtained according to claim 4.

Group IX, claim 62, drawn to nucleic acids encoding variants obtained according to claim 4.

Group X, claims 70,71, drawn to cells containing variants obtained according to claim 4 or containing polynucleotides encoding therefor.

Group XI, claims 74-89, drawn to method of weighting selection rules.

Group XII, claims 91,97, drawn to to variant set, or components thereof, obtained according to claims 75,88.

Group XIII, claims 90,96, drawn to nucleic acids encoding variants obtained according to claims 75,88.

Group XIV, claim 92, drawn to to variant set, or components thereof, obtained according to claims 84.

Group XV, claim 93, drawn to nucleic acids encoding variants obtained according to claims 84.

Group XVI, claim 94, drawn to to variant set, or components thereof, obtained according to claims 86.

**INTERNATIONAL SEARCH REPORT**

International application No.

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Group XVII, claim 95, drawn to nucleic acids encoding variants obtained according to claims 86.

Group XVIII, claims 98-115, drawn to computer software.

Group XIX, claim 116, drawn to computer system.

The inventions listed as Groups I-XIX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Groups directed to "variants" is the technical feature that links Groups I to XIX. The claims of the Groups directed to variants are not the contribution over the prior art because they are suggested by references teaching any sets of substituted biopolymers, e.g., sets of substituted polypeptides. For example, such sets of peptides are taught in US 6,423,686 directed to substituted LHRH derivatives. Therefore, the lack of unity is present because the linking technical feature is not a "special technical feature" as defined by PCT Rule 13.2. Further, the variants of Groups II, V, VIII are not addressed as having common core structure, and are clearly distinct as their structure satisfies different functional requirements. Same for groups directed to corresponding nucleic acids or cells.